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WASHINGTON, D.C. 20460

OFFICE OF  
PREVENTION, PESTICIDES AND  
TOXIC SUBSTANCES

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MEMORANDUM

SUBJECT: Review of Acephate Incident Reports, DP Barcode 247487, Chemical #103301, Reregistration # 0042

FROM: Ruth H. Allen, Ph.D., M.P.H. Environmental Scientist (Health)  
Chemistry and Exposure Branch 1  
Health Effects Division (7509C)

Jerome Blondell, Ph.D., M.P.H., Health Statistician  
Chemistry and Exposure Branch 1  
Health Effects Division (7509C)

THRU: Francis B. Suhre, Senior Scientist  
Chemistry and Exposure Branch 1  
Health Effects Division (7509C)

TO: Felecia Fort, Chemist  
Reregistration Branch 1  
Health Effects Division (7509C)

BACKGROUND

In response to the request that Health Effects Division Epidemiology Group review the incident data on acephate, a search of the published epidemiology literature was conducted, and the following data bases were reviewed for the poisoning incident data on the active ingredient acephate:

1) **OPP Incident Data System (IDS)** - reports of incidents from various sources, including registrants (required under Federal Insecticide Fungicide and Rodenticide Act (FIFRA) Section 6(a)(2)), other federal and state health and environmental agencies and individual consumers, submitted to OPP since 1992. Reports submitted to the Incident Data System represent anecdotal reports or allegations only, unless otherwise stated. Typically no conclusions can be drawn implicating the pesticide as a cause of any of the reported health effects. Nevertheless, sometimes with enough cases and/or enough documentation risk mitigation measures may be suggested.

2) **American Association of Poison Control Centers (AAPCC)** - as the result of Data-Call-Ins issued in 1993, OPP received Poison Control Center data covering the years 1985 through 1992 for 28 organophosphate and carbamate chemicals. Most of the national Poison Control Centers (PCCs) participate in a national data collection system, the Toxic Exposure Surveillance System which obtains data from about 60-70 centers at hospitals and universities. PCCs provide telephone consultation for individuals and health care providers on suspected poisonings, involving drugs, household products, pesticides, etc. In addition, EPA purchased data for the time period 1993-1996 for all pesticides.

3) **California Department of Pesticide Regulation** - California has collected uniform data on suspected pesticide poisonings since 1982. Physicians are required, by statute, to report to their local health officer all occurrences of illness suspected of being related to exposure to pesticides. The majority of the incidents involve workers. Information on exposure (worker activity), type of illness (systemic, eye, skin, eye/skin and respiratory), likelihood of a causal relationship, and number of days off work and in the hospital are provided.

4) **National Pesticide Telecommunications Network (NPTN)** - NPTN is a toll-free information service supported by OPP. A ranking of the top 200 active ingredients for which telephone calls were received during calendar years 1984-1991, inclusive has been prepared. The total number of calls was tabulated for the categories human incidents, animal incidents, calls for information, and others.

## ACEPHATE REVIEW

### I. Incident Data System

There are two types of incident information on file for acephate: (A) *Report of the Investigation of the Death of (name withheld)* by Sheldon L. Wagner, M.D. Letter to Jerome Blondell, Office of Pesticide Programs, September 3, 1998, and (B) routine reporting to the Incident Data System (IDS).

#### A. *Report of the Investigation of the Death of (name withheld)* by Sheldon L. Wagner, M.D.

A 24 year old male pesticide applicator with no prior history of any cardiac difficulties died suddenly after spraying seven homes with a mixture of acephate and dicofol. A medical review of the applicator's autopsy report, clinical toxicology findings, and results of cholinesterase tests on his tissues were requested by EPA. Dr. Wagner, Professor of Clinical Toxicology at Oregon State University and medical advisor to the Epidemiology Group concluded that "the most probable cause of death was an acute ventricular fibrillation resulting from organophosphate exposure and intoxication."

On the day of his death, the pesticide applicator was mixing and applying organophosphate insecticide without proper protection, and with a particulate mask that would have increased his risk of inhaling increased concentrations of the insecticide. At the seventh home he sprayed, he complained of headaches and collapsed. Attempts to resuscitation failed and he was declared dead one half hour after admission to the emergency room. His stomach contents and urine were negative for drugs and other substances. Dr. Wagner concluded that he had died with documented ventricular fibrillation, the most common type of cardiac arrhythmia occurring with organophosphate insecticides.

Details of the lab assay methods and storage stability of the enzymes were reviewed with three authorities, and these findings and the presence of anticoagulants EDTA was evaluated by Dr. Wagner who concluded that “an abnormally low cholinesterase confirmed significant exposure and /or intoxication from acephate.” Dr. Wagner concluded that “the most probable cause of death was an acute ventricular fibrillation resulting from organophosphate exposure and intoxication.”

#### B. Incident Data System (IDS) Routine Reporting for Acephate.

Acephate human poisoning incidents are reported for multiple geographic locations, by several companies, and for a variety of uses and formulations. Only those cases involving a moderate, major, or fatal outcome are summarized below. Certain large compilations of cases (e.g., packages numbered 1264, 1827, 3268, 3326, 3380, 3474, 3844, and 4007) that duplicate information collected by Poison Control Centers and covered elsewhere in this review are also excluded from the section below.

##### Incident #732-1

In September 1992, in Florida a female scout in tomato fields developed dizziness, weight loss, headaches, vomiting, spots before her eyes. She did not seek medical attention immediately, but symptoms persisted and she was hospitalized a few days or weeks later (time not specified). Some of her symptoms have reportedly persisted for months since this incident. No further information on the disposition of this case is available.

##### Incident #2969-5

In 1995 an incident was reported involving inhalation and respiratory irritation that was classified as having a moderate outcome. No further information on the disposition of this case is available.

##### Incident #2969-7

In 1995 an incident occurred where inhalation of acephate reportedly led to headache, difficulty breathing, and pain in the chest. No further information on the disposition of this case is available.

##### Incident #2969-34

In 1995 an incident occurred when a human was exposed (route of exposure unknown)

and became semi-conscious. No further information on the disposition of this case is available.

#### Incident #2969-59

In an undescribed incident which led to a lawsuit, an injury was alleged from re-entering a place where acephate had been used. No further information on the disposition of this case is available.

#### Incident #3599-1

The Minnesota Department of Agriculture surveyed state enforcement agencies to determine what pesticides were involved in spray drift. Among the 32 states responding to the survey, there were a total of 2,681 cases of drift complaint. Acephate was responsible for 19 complaints or about one percent of the total.

#### Incident #4535-1

An incident occurred in 1996 when dermal exposure to a 62 year old led to lethargy, coughing/choking, pulmonary edema, respiratory irritation, and fever. No further information on the disposition of this case is available.

## II. Poison Control Center Data - 1985 through 1992

Acephate was one of 28 chemicals for which Poison Control Center (PCC) data were requested. The following text and statistics are taken from an analysis of these data; see December 5, 1994 memo from Jerome Blondell to Joshua First.

The 28 chemicals were ranked using three types of measures: (A) number and percent occupational and non-occupational adult exposures reported to PCCs requiring treatment, hospitalization, displaying symptoms or serious life-threatening effects; (B) ratios of poisonings and hospitalization for PCC cases to estimated number of containers used in U.S. homes; and [C] number and percent of child exposures to PCCs requiring treatment, hospitalization, displaying symptoms or serious life-threatening effects.

### A. Occupational and Non-occupational Exposure

From 1985-1992, there were a total of 3,004 acephate cases in the PCC data base. Of these, 334 cases were occupational exposure; 208 (62%) to acephate alone and 126 (38%) involving exposure to multiple products including acephate. There were a total of 1,996 exposures to adults and children six years old or older; 1,753 (88%) involving acephate alone and 243 (12%) with multiple products.

In this analysis, four measures of hazard were developed based on the Poison Control Center data, as listed below.

1. Percent of all accidental cases that were seen in or referred to a health care facility (HCF).
2. Percent of these cases (seen in or referred to HCF) that were admitted for medical care.
3. Percent of cases reporting symptoms based on just those cases where the medical outcome could be determined.
4. Percent of those cases with outcome determined that had a major medical outcome (defined as life-threatening or permanent disability) or death.

Exposure to acephate alone or in combination with other chemicals was evaluated for each of these categories, giving a total of 8 measures. A ranking of the 28 chemicals was done based on these measures with the lowest number being the most frequently implicated in adverse effects. Table 1 presents the analyses for occupational and non-occupational exposures.

Table 1. Measures of Risk From Occupational and Non-occupational Exposure to Acephate Using Poison Control Center Data from 1985-1992<sup>a</sup>

	Occupational Exposure	Non-occupational Exposure
Percent Seen in HCF		
Single product exposure	63.0 (68.2)	27.7 (44.0)
Multiple product exposure	66.5 (69.8)	29.8 (46.1)
Percent Hospitalized		
Single product exposure	12.2 (12.2)	6.0 (9.9)
Multiple product exposure	14.9 (14.3)	6.9 (12.6)
Percent with Symptoms		
Single product exposure	87.9 <sup>*7</sup> (85.8)	67.5 (74.0)
Multiple product exposure	87.8 (85.8)	69.8 (75.2)
Percent with Life-threatening Symptoms		
Single product exposure	0.8 <sup>b</sup> (0.0)	0.2 <sup>b</sup> (0.0)
Multiple product exposure	0.5 <sup>b</sup> (0.5)	0.3 <sup>b</sup> (0.05)

a Extracted from Tables 2, 3, 5 and 6 in December 5, 1994 memo from Jerome Blondell to Joshua First; number in parentheses is median score for that category.

b The percents calculated for the occupational category are based on a single life-threatening case. For non-occupational exposures to a single product, there were 2 life-threatening cases and 1 fatality. The percents calculated for non-occupational exposure to multiple products, included these 3 cases plus 2 more life-threatening cases.

\* Top 25% of chemicals are ranked with a superscript of 1 to 7

Compared to other organophosphate and carbamate insecticides, acephate generally similar or somewhat below median levels for health care requirements and occurrence of

symptoms. However, for life-threatening or fatal cases, the percents are above the median. The one fatality due to acephate was reported in 1990 involving a 67 year old who was exposed by route of inhalation due to accidental misuse.

#### B. Ratios of Poisoning - U.S. Poison Control Data

Active registrations of acephate include significant residential uses. A comparison was computed for ten pesticides with significant home use between number of non-occupational exposures, poisonings and health care referral and the number of containers reported in U.S. homes. The results for acephate and the median for all 10 residential cholinesterase inhibitors included in the analysis are presented in the Table 2 below.

Table 2. Ratios of acephate exposures, poisonings, and cases referred to a health care facility (PCC Data, 1985-1992) to reported use in U.S. homes in 1990 (children under age six excluded)<sup>a</sup>

Pesticide	Exposure Per Use	Poisonings Per Use	Health Care Referral Per Use
Acephate	.461	.183	.150
Median	.790	.312	.320

<sup>a</sup> Extracted from Table 9 in the December 5, 1994 memo from Jerome Blondell to Joshua First

\* Top 33% of chemicals are ranked with a superscript of 1 to 5

Among pesticides used widely in residential areas, acephate had ratios that were close to half the median (Table 2).

#### C. Exposure in Children

A separate analysis of the number of exposures in children five years of age and under from 1985-1992 was conducted. For acephate, there were 674 incidents; 575 (85%) involved exposure to acephate alone. Compared to 16 other organophosphates and carbamates that 25 or more children were exposed to acephate cases were less likely to require medical attention. Acephate was also slightly less likely to result in related symptoms and there were no life-threatening or fatal cases in children under six years of age.

Poison Control Center Data - 1993 through 1996

Results for the years 1993 through 1996 are presented below for occupational cases, non-occupational involving adults and older children, and for children under age six. Unlike the earlier analysis for 1985-1992, cases involving exposures to multiple products are excluded. This is because the earlier analysis showed little difference in rankings and measurement of hazard when multiple exposure cases were included. Tables 3-5 present the hazard information for acephate compared with all other pesticides on six measures: percent with symptoms, percent with moderate, major, or fatal outcome, percent with major or fatal outcome, percent of exposed cases seen in a health care facility, and percent hospitalized and percent seen in a critical care facility. Table 3 presents this information for occupational cases, Table 4 for non-occupational cases involving adults and older children (six years or older), and Table 5 for children under age six.

Table 3. Comparison between acephate and all pesticides for percent cases with symptomatic outcome (SYM), moderate or more severe outcome (MOD), life-threatening or fatal outcome (LIFE-TH), seen in a health care facility (HCF), hospitalized (HOSP), or seen in an intensive care unit (ICU) reported to Poison Control Centers, 1993-1996 for occupational cases only.

Pesticide	SYM*	MOD*	LIFE-TH*	HCF*	HOSP*	ICU*
Acephate	91.3%	20.3%	0%	46.0%	12.5%	9.38%
All Pesticides	85.9%	18.8%	0.60%	46.8%	7.18%	2.89%

\* Symptomatic cases based on those cases with a minor, moderate, major, or fatal medical outcome. Denominator for SYM, MOD, and LIFE-TH is the total cases where medical outcome was determined. Denominator for HCF is all exposures. Denominator for HOSP and ICU is all cases seen in a health care facility.

Table 4. Comparison between acephate and all pesticides for percent cases with symptomatic outcome (SYM), moderate or more severe outcome (MOD), life-threatening or fatal outcome (LIFE-TH), seen in a health care facility (HCF), hospitalized (HOSP), or seen in an intensive care unit (ICU) reported to Poison Control Centers, 1993-1996 for non-occupational cases involving adults and older children.

Pesticide	SYM*	MOD*	LIFE-TH*	HCF*	HOSP*	ICU*
Acephate	69.5%	9.79%	0.16%	23.2%	9.43%	4.04%
All Pesticides	70.8%	10.8%	0.34%	18.7%	7.62%	3.36%

\* Symptomatic cases based on those cases with a minor, moderate, major, or fatal medical outcome. Denominator for SYM, MOD, and LIFE-TH is the total cases where medical outcome was determined. Denominator for HCF is all exposures. Denominator for HOSP and ICU is all cases seen in a health care facility.

Table 5. Comparison between PCP and all pesticides for percent cases with symptomatic outcome (SYM), moderate or more severe outcome (MOD), life-threatening or fatal outcome (LIFE-TH), seen in a health care facility (HCF), hospitalized (HOSP), or seen in an intensive care unit (ICU) for adults and children six years and older reported to Poison Control Centers, 1993-1996 for children under six years old.

Pesticide	SYM*	MOD*	LIFE-TH*	HCF*	HOSP*	ICU*
Acephate	23.5%	1.53%	0%	15.0%	5.56%	1.85%
All Pesticides	22.3%	1.48%	0.13%	17.5%	5.47%	1.61%

\* Symptomatic cases based on those cases with a minor, moderate, major, or fatal medical outcome. Denominator for SYM, MOD, and LIFE-TH is the total cases where medical outcome was determined. Denominator for HCF is all exposures. Denominator for HOSP and ICU is all cases seen in a health care facility.

For non-occupational cases involving adults and older children or young children, acephate has a similar hazard profile to all other pesticides. Whether examining the symptomatic measures (SYM, MOD and LIFE-TH in the tables above) or health care-related measures (HCF, HOSP, and ICU) acephate had almost the same degree of hazard or perhaps a bit less hazard (e.g., health measures in Table 5). In contrast, hazards were noticeably higher for individuals exposed to acephate occupationally. This difference, however, was mostly limited to health care measures. Occupational acephate cases were 74% more likely to require hospitalization and three times more likely to be treated in an intensive care unit.

### III. California Data - 1982 through 1995

Detailed descriptions of 259 cases involving acephate submitted to the California Pesticide Illness Surveillance Program (1982-1995) were reviewed. In 89 of these cases, acephate was judged to be responsible for the health effects. Only cases with a definite, probable or possible relationship were reviewed. Acephate ranked 22nd as a cause of systemic poisoning in California. Table 6 presents the types of illnesses reported by year. Table 7 gives the total number of workers that took time off work as a result of their illness and how many were hospitalized and for how long.



Table 6. Cases Due to Acephate Exposure in California Reported by Type of Illness and Year, 1982-1995

Year	Illness Type				
	Systemic <sup>b</sup>	Eye	Skin	Respiratory	Total
1982	5	1	-	-	6
1983	3	2	1	-	6
1984	-	2	1	-	3
1985	2	1	-	-	3
1986	10	4	1	-	15
1987	1	1	-	-	2
1988	20	1	1	-	22
1989	2	1	1	-	4
1990	3	-	2	1	6
1991	8	-	-	-	8
1992	-	2	-	-	2
1993	1	3	-	-	4
1994	3	-	-	-	3
1995	4	-	-	1	5
Total	62	18	7	2	89

<sup>b</sup> Category includes cases where skin, eye, or respiratory effects were also reported

<sup>c</sup> Category includes combined irritative effects to eye, skin, and respiratory system

A total of 62 persons had systemic illnesses or 70% of 89 persons. A total of 22 workers took time off work as a result of their exposure to acephate, as shown in Table 7 below. A variety of worker activities were associated with exposure to acephate as illustrated in Table 8 below.

Table 7. Number of Persons Disabled (taking time off work) or Hospitalized for Indicated Number of Days After Acephate Exposure in California, 1982-1995.

	Number of Persons Disabled	Number of Persons Hospitalized
One day	10	-
Two days	5	-
3-5 days	5	-
6-10 days	1	-
more than 10 days	1	-
Unknown	2	1

Table 8. Illnesses by Activity Categories for Acephate Exposure in California, 1982-1995

Activity Category	Illness Category				
	Systemic <sup>b</sup>	Eye	Skin	Respiratory	Total
Applicator	14	12	4	-	30
Mixer/Loader	-	3	-	1	4
Coincidental	3	-	-	-	3
Drift exposure	8	1	-	-	9
Field Residue	8	-	1	-	9
Other residue <sup>a</sup>	11	1	1	-	13
Manuf./Formulator	3	-	-	-	3
Other occupational	2	1	1	-	4
Non-occupational	13	-	-	1	14
Total	62	18	7	2	89

<sup>a</sup> Other Residue = worker exposed to residue neither agricultural nor structural.

<sup>b</sup> Category includes cases where skin, eye, or respiratory effects were also reported.

According to the above activity categories, applicators and other handlers accounted for

over a third of the illnesses. Significant number of illnesses were also reported for workers exposed to spray drift and field residue. These illnesses included symptoms of dizziness, nausea, vomiting, chest tightness, eye and skin irritation, skin rashes, and incoordination.

One of the most common causes of acephate poisonings according to the California reports were spills in enclosed spaces, often from broken glass bottles. Approximately, one-third of the systemic illnesses could be ascribed to this cause.

#### Ratios of poisoning - California Data

The incidence of **systemic poisoning cases** in agricultural workers reported to the California was compared to the number of applications of acephate. Those calculations, along with the median score for a total of 29 pesticides, are presented in the Table 9 below.

Table 9. Systemic Poisonings/1,000 Applications in Selected Agricultural Workers Exposed to Acephate in California, 1982-1989<sup>a</sup>

Pesticide	Number of Applications	Poisonings/1,000 Applications (N) Primary Pesticide Only			Poisonings/1,000 Applications (N) Multiple Pesticide Exposure		
		Handlers	Field Workers	Total	Handlers	Field Workers	Total
Acephate	84,433	.04 (3)	.13 (11)	.17 (14)	.20 (17)	.20 (17)	.40 (34)
Median		.21	.20	.41	.44	.50	1.02

<sup>a</sup> Extracted from Table A5 in December 5, 1994 memo from Jerome Blondell to Joshua First; number in parentheses is the observed number of poisoned cases.

Acephate was not among the top five in ratio of field worker poisonings per 1,000 applications in California (see Table 7 in the December 5, 1994 memo.). Generally, the ratio of poisoning per thousand applications was well below the median, 80% lower for handlers and 35% lower for field workers exposures to acephate as the primary pesticide.

California accessed medical monitoring records for 542 agricultural pesticide applicators under medical supervision in 1985 for exposure to the more toxic cholinesterase-inhibiting organophosphate and carbamate pesticides (Ames et al. 1987, 1989). In California, cholinesterase monitoring is required for all pesticide applicators who handle Toxicity Category I or II organophosphate or carbamate pesticides for 30 hours or more in any 30 day period. To be included in the survey, the worker had to have at least one pre-exposure (baseline) cholinesterase measurement and at least one exposure value (mid-season). A data-call-in was issued by the California Department of Food and Agriculture and local Agricultural Commissioners through pesticide application firms to their medical supervisors. Follow up letters were sent and phone calls made to employers, physicians, and laboratories performing tests, but significant under reporting is

likely to have occurred. Therefore, these workers may not be representative of all workers undergoing medical monitoring in California. However, they do represent exposure effects verified by medical laboratories. Cholinesterase activity depression of 20 percent or more below baseline was observed in 127 or 23 percent of the 542 workers. Depression of 20 percent or more below baseline represents strong evidence of exposure (Gallo and Lawryk 1991).

Specific pesticide exposure was available for 94 of the 127 cases, based on usage records for the previous two weeks. Of these, 31 percent had been exposed to mevinphos, 21 percent to methomyl, and 21 percent to parathion, the three leading pesticides responsible for cholinesterase inhibition. Of the 94 cases with inhibition, 16% had exposure in the past two weeks to acephate. Note that many of the workers were exposed to two or more pesticides during the two weeks before they had cholinesterase depression of 20% or more. Twelve of the workers in this study were reported to have pesticide-related illnesses by their physicians. These data demonstrate that agricultural workers, who mix, load and apply the more toxic pesticides are subject to significant levels of exposure despite the considerable restrictions in place to prevent exposure.

#### IV. NPTN

On the list of the top 200 chemicals for which NPTN received calls from 1984-1991 inclusively, acephate ranked number 13 and was reported to be involved in 254 human incidents and 24 animal incidents.

#### V. Summary/Conclusions

When both Poison Control Center and California data were considered, acephate generally had a lower hazard than other organophosphate and carbamate insecticides. There have been two accidental deaths reported associated with exposure. Both deaths involved misuse and in one case use of a particulate mask may have increased the risk of inhaling acephate. Minor and moderate symptoms of exposure have often been associated with inhalation indoors. Outdoor agricultural use are associated with lower risks of illness and poisoning than most other organophosphate and carbamate insecticides.

#### VI. Recommendations

Indoor use of acephate should be restricted to certified Pest Control Operators. Homeowner products should be limited to only products that are either ready-to-use or mostly diluted product. The one exception to this should be hose-end sprayers and other concentrates that can be used by homeowners without mixing or pouring. Acephate should be sold in non-breakable containers.

#### References

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cc: Correspondence  
Acephate file (chemical no. 103301)  
Jack Arthur - 7509C  
Monica Alvarez - 7508W